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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,876	11/17/2003	Jerrold P. Weiss	17023-030001/ 03067	5262

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VIKSNINS HARRIS & PADYS PLLP
P.O. BOX 111098
ST. PAUL, MN 55111-1098

EXAMINER

AUDET, MAURY A

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/715,876

Applicant(s)

WEISS ET AL.

Examiner

Maury Audet

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/18/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. (2003/0175762).

Schwartz et al. teach administration of purified endotoxin (also known as lipopolysaccharide (LPS), wild-type or gram-negative bacterial) and MD-2 (both administered into a THP-1 cell containing TLR4, forming a complex therein) for the purpose of binding to TLR4 to produce TLR-4 dependent activation of the cell (para's 10, 19); which is soluble in water (inherent based on administration to cell, which is in a liquid state), in a composition with a pharmaceutically acceptable carrier (inherent since MD-2 is administered as part of a mixture and endotoxin in a ng/ml dose, wherein the ml content is in the context of a carrier). Schwartz et al. does not expressly teach that the endotoxin is bound to MD-2; or that expressly the various bacterium from which endotoxin may emanate, a complex molecular weight of 25,000, that half/less the TLR4 activation is directed, or the endotoxin acylation species.

Khan et al. (2003/0119720) teach TLR4 is activated for signaling by both LPS and MD2 (para. 74).

Calandra et al. (2002/0192217) teach that MD2 is a secreted protein that associates with the extracellular domain of TLR4 and augments the cell response to LPS.

Art Unit: 1654

Nunez et al. (2203/0175762) teach that expression of TLR4 does not produce activation by LPS alone, which is consistent with recent reports that additional cell surface molecules such as MD2 are required for TLR4 mediated LPS response in cells (para 384).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer LPS and MD2 in a bound form, rather than singular form, in Schwartz et al., because Khan et al, Calandra et al., and Nunez et al., all teach the advantageous synergistic effect of LPS and MD2 on TLR4 signaling, and because Schwartz et al. teach the singular administration of LPS and MD2 for the same effect. Thus, one of ordinary skill in the art would be motivated to administer LPS and MD2 in bound form (or singular form), in order to elicit the synergistic signaling effect desired in the TLR4 pathway.

Additionally, it would have been obvious to one of ordinary skill in the art at the time of the invention to use an endotoxin from various bacterium from which endotoxin may emanate, a complex molecular weight of 25,000, half/less the TLR4 activation, or endotoxin acylation species in the complex of Schwartz et al. because Schwartz et al. teach the advantageous administration of both endotoxin into a TLR4 containing cellular medium, and the choice bacterium to produce the endotoxin, amount of the components, degree of activation, and degree of endotoxin acylation are merely routine optimization by one of skill in the art, absent evidence to the contrary.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at

Art Unit: 1654

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

MA, 07/08/05


CHRISTOPHER R. TATE
PRIMARY EXAMINER